Diabetes surgery in type 2 BMI 24-29 vs IMC 30-34 diabetic patients: is there differences among restrictive, malabsorptive and gastric bypass procedures?

M. GarcíaCaballero¹, S. Navarrete², F. Favretti³, A. Celik⁴ and D. Del Castillo⁵


Abstract

Diabetes mellitus (DM) is a public health problem with a prevalence of 345 million people worldwide that it may double by the year 2030 and have a high costs and mortality. Gastrointestinal surgery is accepted as a form of treatment that was already suggested for obese in 1987 by Pories, confirmed for obese patients by the meta-analysis of Buchwald and the direct comparison of gastric bypass with medical treatment in the study of Schauer that demonstrate a 4 fold greater resolution rate of DM with surgery. Improvement occurs immediately after surgery, before the patients lose weight in with BMI > 35; but there is doubt if the existent evidence is enough to extrapolate these results to patients with BMI < 35 and especially with BMI < 30, in spite that four reviews in patients with this BMI and DM2 demonstrated the same results when stomach, duodenum and part of jejunum is bypassed as happen gastric bypass (better results with this of one anastomosis than of two anastomosis, Roux-en-Y) BPD. For patients with a BMI between 30 and 35 restrictive techniques: LAGB and SGL are good but not better than the mixed: KYGB, BAGUA, or SG-DJB with remission from 60 to 100 %, minor in the derivative: BPD and above on the IID with a 81 % of remission. There are no differences in the metabolic control in comparison to the obese, It is progressively better with DJB, SDS, IID and BAGUA especially in patients who do not require insulin, have less time with disease, have normal C peptide levels, and not so much relation with the initial BMI that is only important to decide the degree of restriction. Although several mechanisms has been suggested for explaining these results such as caloric intake, hormonal changes, bypass of the anterior or early stimulation of posterior intestine, fundectomy, intestinal gluconeogenesis and others, new ones will appear in the near future.

Key words: Diabetes surgery BMI 24-34. Restrictives bariatric procedures. Malabsorptive bariatric procedures.

CIRUGÍA EN PACIENTES CON DIABETES TIPO 2 IMC 24-29 VS IMC 30-34: ¿EXISTEN DIFERENCIAS ENTRE LOS PROCEDIMIENTOS RESTRICTIVOS, MALABSORTIVOS Y BYPASS GÁSTRICO?

Resumen

La diabetes mellitus (DM) es un problema de salud pública, con una prevalencia de 345 millones de personas, que puede duplicarse para el año 2030 y con importante repercusión en costes y mortalidad. La cirugía gastrointestinal es aceptada como una forma de tratamiento sugerida en obesos desde 1987 por Pories, y confirmada por el meta-análisis de Buchwald y la comparación directa del bypass gástrico con el mejor tratamiento médico en el estudio de Schauer que pone de manifiesto una relación de remisión 4 veces mayor con la cirugía. La mejora ocurre inmediatamente después de la cirugía, antes de la pérdida de peso en pacientes con IMC > 35; pero hay duda si la evidencia existente es suficiente para extrapolar estos resultados a pacientes con IMC < 35 y especialmente con IMC < 30, a pesar de existir cuatro revisiones en pacientes con este IMC y DM2 que demuestran los mismos resultados que en obesos cuando se puentea estómago, duodeno y parte del yeyuno como pasa en el bypass gástrico y la DBP. Para pacientes con IMC entre 30 y 35 las técnicas restrictivas: BGL AL Y GVL son buenas pero no superiores a las mixtas: BGYR, BAGUA o GV-BDY con remisión desde 60 a 100 %, menor en las derivativas: DBP y mayor en la IID con un 81 % de remisión. En pacientes con sobrepeso no existen diferencias en el control metabólico respecto a los obesos. Es progresivamente mejor con DBP, CDC, IID y BAGUA sobre todo en pacientes que no requieren insulina, tienen menos tiempo con la enfermedad o con un nivel de peptido C normal, factores determinantes y no así el IMC inicial que sólo influye en el volumen de restricción. Aunque se han sugerido distintos mecanismos para explicar los resultados como ingesta calórica, hormonales, teoría del intestino anterior o posterior, fundectomía, neoglucogénesis intestinal y otros, aparecerán más en un futuro no lejano.

Key words: Cirugía diabetes IMC 24-34. Procedimientos bariátricos restrictivos. Procedimientos bariátricos malabsortivos.

Correspondence: Manuel GarcíaCaballero.
Full Professor of Surgery.
University of Málaga.
Medical Faculty
29080 Málaga. Spain.
E-mail: gcaballe@uma.es
Introduction

Diabetes Mellitus (DM) is at present an important health problem and gastrointestinal surgery is every time a more accepted solution as was hypothesized some years ago. However, the great number of patients suffering DM make impossible to operate all of them and we need to choose those that can obtain the best benefit from the gastrointestinal changes performed by surgery for solving DM.

World Health Organization (WHO) advise that there are 346 millions people affected by Diabetes mellitus Type 2 and this number could be duplicated for the 2030 if we do not take special care to prevent it. This illness is the responsible for 5% of all deaths over the world and we need to emphasized that there are a lot of cases undiagnosed and it could reach 4 to 6% (USA vs Spain) and this is the reason why we need to use the diagnosis criteria as ADA mention (126 mg/dl in fasting glycemia,...), also use the HbA1c as the best marker to follow the evolution of the disease because it is a good expression of the illness control and we know HbA1c is an oxidative product of glucose metabolism and could be deleterious above 7% because below this level the endothelium has the same evolution as the normal subjects.

For obese patients the surgical criteria are clear and unanimous accepted.

Since 1987 when Pories started to publish their papers about the diabetes mellitus evolution in obese patients after the Greenville gastric bypass, where he mentioned that it could be possible that arrangements in the gastrointestinal tract as gastric bypass were the responsible of the improvement of the disease, a lot of studies have appeared that try to clarify that question. The positive effect of bariatric procedures (mostly gastric bypass) has been confirmed by meta-analysis, which demonstrated the superiority of the biliopancreatic diversion procedures as gastric bypass and BPD without or with duodenal switch over the restrictive procedures. And also direct randomized studies comparing gastric bypass and sleeve gastrectomy versus the best medical treatment, demonstrating in this case the superiority of gastric bypass over sleeve gastrectomy (42% vs 37% of the patients with glycated hemoglobin < 6% 12 months after surgery), as well as the superiority of both over intensive medical treatment (only 12% of the patients with glycated hemoglobin < 6%).

However, so far, there is not the same certainty for extrapolating the results obtained in morbid obese to patients with BMI < 35. Although the experience on the resolution of DM type 2 by bariatric surgery reported until now demonstrate that the effect is seen immediately after surgery, before weight loss happens and, hence, not direct related with the preoperative weight of the patient. The general idea is that obese patients could have more benefit from bariatric surgery based on the assumption: more obesity come to more insulin resistance than beta cell mass deficit and, hence, more possibility of diabetes resolution by the weight loss produced by bariatric surgery. While less obesity would speak on more beta cell deficit than insulin resistance and less possibility of resolution by bariatric surgery. But these pathophysiological deductions need to be confirmed by the evidence, especially if we consider our ignorance on the mechanisms responsible of the results we obtain by gastrointestinal surgery in BMI < 35 diabetic patients.

The other uncertainty in relation with the surgical treatment of DM in patients BMI < 35 is, which gastrointestinal surgical changes could have more and/or better effect on the diabetes resolution.

We analyze separately patients with BMI30-34 and those with BMI below 30, emphasizing the postoperative change of some variables as HbA1c, Fasting Glycemia, Dyslipidemias, its relation with the bariatric surgery procedures used, as well as the limitations of the data supplied in the studies.

Results of bariatric surgery use primary for treating diabetes in patients BMI 30-34

It has been published four reviews on the role of bariatric-metabolic surgery in the treatment of type 2 diabetes with BMI < 35. All four reviews included the same studies. The difference is that the first one included only 13 of them, the second 14, 16 studies and 343 patients the third and the last published in 2012 included 29 studies with 1,209 patients. As in the case of obese diabetic patients, overall the percentage of resolution of DM is superior for the procedures that bypass most of the stomach, duodenum and part of the jejunum than for the restrictive procedures. But in this case the better results are obtained for gastric bypasses of one anastomosis (One Anastomosis Gastric Bypass —BAGUA— and Mini Gastric Bypass —MGB—) over Roux-en-Y Gastric Bypass and pure malabsorptive procedures.

Restrictive procedures

The first paper that reported the results on the effect of a bariatric restrictive procedure to treat Metabolic Syndrome was O’Brien using lap-band in 2006. Before that, Angrisi in 2004 and Parikh in 2006 published their series using lap-band but they only mentioned patients with lost weight and those who have DM2 (4 and 8 respectively). O’Brien et al. compared the results obtained through an adjustable gastric band surgery versus medical treatment based on a very-low-calorie diet, use of drugs (Orlistat®), and a supervised program of change of habits and behavior as well as physical activity in 80 patients with a 24-month follow-up.

While this is not a specific study on type 2 diabetes, 37.5% of patients had a diagnosis of metabolic syn-
drome (MS) according to the ATP III criteria, which is closely linked to disorders in the glucose metabolism. The results of this series reflected that MS persisted in only 2.7% of patients after surgical treatment, while it persisted in 24% of patients undergoing medical treatment. Regarding excess weight loss, it was of 87.2% in the group that underwent the surgical procedure vs. 21.8% in the group subject to medical treatment (p < 0.001). Then in 2009 Sultan et al. did the same, publishing their results but again he did not inform about DM2. He just mentioned the number of patients with the disease. One year later Lee published that SGL could improve FPG and HbA1c (240,1 to 132,9 and 10.1 to 7,1 respectively) and the changes are loss weight related.

**Mixed procedures**

Analyzing the studies reporting results with mixed procedures we observe that since 2006 when Cohen published his first paper until 2008 with Lee, we do not find anyone. After that appeared eight new studies in USA, Latin América, Asia and Europe (De María, Shah, Huang, Lee, Boza, DeSa, Navarrete and García-caballero) presenting similar results in BMI and weight loss, FPG and HbA1c.

In 2006, Cohen et al published their experience with Roux-en-Y Gastric Bypass in type 2 diabetes patients with class I obesity. This is a prospective study with 37 patients and average follow-up of 20 months in which all patients were treated before operation by oral anti-diabetic drugs without insulin. The patients were also hypertensive and dyslipidemic. After the procedure, there was 100% remission of diabetes (fasting glucose values normal without medical treatment, and glycosylated hemoglobin [HbA1c] < 6%) and 36 patients showed remission of all related co-morbidities. There was no morbidity and no patient had an excessive weight loss.

According to data obtained from the American Society for Metabolic and Bariatric Surgery through its Centers of Excellence program, between 2007 and 2009, there were 235 patients reported with a BMI < 35 who underwent metabolic surgery to treat type 2 diabetes in the United States; ninety two percent of patients overweight or with mild obesity and they showed a 100% remission of diabetes in 93% of the subjects. García Caballero et al. reporting on 60 patients, 35 of whom were BMI 30-34 (11 non insulin dependent and 24 insulin dependent) and 25 BMI 24-29 (9 non insulin dependent and 16 insulin dependent) find a mean resolution (postoperative HbA1c < 7% + resolution DM+MS without any treatment) rate of 67%. But when they analyzed separately non insulin dependent patients found a 100% resolution rate while in insulin dependent patients there were 50% resolution, 22,5% improvement needed only with oral anti-diabetic drugs and 27,5% move from 3-4 rapid insulin and 1 or 2 delayed insulin injections/day to only one of very reduced dose of delayed insulin/ day. These data demonstrated the importance of given precise information on the preoperative diabetes situation of the patients to be able to evaluate the effect of the different gastrointestinal surgical changes in diabetes resolution or improvement as was already discussed in the editorial of this monographic issue. They do not find difference in the results between patients related with the preoperative BMI 30-34 and BMI 24-29.

It seems, then, that in the last two years, sufficient clinical evidence of the benefits and low risk of the laparoscopic gastric bypass has emerged in the management and treatment of DM, regardless of the approximated size of the gastric pouch: 15 ml (29), 30 ml (27,22) or 50 ml (10,11) or the length of the intestinal limbs: biliopancreatic 50 cm, 100 cm, 26 100-150 cm in one anastomosis and mini gastric bypass; or alimentary 100 cm or 150 cm. But not only RYGB or One Anastomosis and Mini Gastric Bypass have these mechanisms, also a new technique was proposed by Alamo et al. doing a Sleeve Gastrectomy with a distal Jejunal Bypass preserving the duodenal absorption and 200 cm common channel. They reported 81,6% complete remission.

**Malaabsorptive procedures**

In 1998 Noya et al published the first serie of 10 patients with type 2 diabetes, and class I obesity (mean BMI 33,2) who underwent a biliopancreatic diversion with gastric preservation. They observed normal blood glucose values and a mild weight loss in nine patients within the first postoperative weeks. In 2007 Scopinaro et al published a retrospective analysis with 7 patients with type 2 diabetes and BMI < 35 who had undergone a biliopancreatic diversion. Although this was a small serie had a follow-up of 13 years, making it the only one reporting long-term results up to this date. Diabetes was controlled by 28,5% and improved by 100% without medical treatment, and no patient had undesirable weight loss. Recently the same group published the results of a prospective controlled study comparing the effects of BPD in type 2 diabetic patients overweight or with mild obesity and they showed an improvement of HbA1c and FSG in com-
parison with the control group one and 2-years after surgery, confirming the superiority of BPD to standard medical care. They also conclude that it exists a significant difference between the BMI ranges 25-30 and 30-35 in BPD effect on glycemic control, and thus in the biological severity of the disease, giving additional information on the related consequences.

The ileal interposition

First performed by De Paula, Ileal Interposition with sleeve gastrectomy comprises of a gastric sleeve with inter-positioning of a segment of ileum in to jejunum. The operation can be performed in two ways: with or without diversion of the duodenum. In the non-diverted version the ileal segment is interposed to the proximal jejunum (termed Jejuno-Ileal Interposition JII). Therefore there is absolute no malabsorption. In the diverted version, the duodenum is diverted from 2-3 cm distal to the pylorus and the ileal segment is interposed in between the distal part of the sleeve and proximal jejunum, thereby bypassing the duodenum and the proximal jejunum (termed Duodeno-Ileal Interposition DII).

De Paula et al have a lot of experience with interesting results, better with DII than with JII. In his first paper with 39 patients BMI below 35 (mean BMI = 30.1, range, 23.4-34.9), using the two laparoscopic procedures described above with mean operative time of 185 min, mortality rate 2.6%, and an adequate glycemic control in 86.9%. In 2010 they published a randomized controlled trial including 38 patients BMI below 30 (JII 27 vs DII 29.9) comparing both operations, with better results for DII: remission rate was 81.3% DII vs 35.3% JII and HbA1c 5.39% DII vs 6.31% JII and they concluded that both operations were safe and effective for controlling type 2 DM in a nonobese (BMI 21-34) population.

Experience with bariatric surgery for treating diabetes in patients BMI < 30

That is from the beginning the most controversial group based on the pathophysiological deductions mentioned above: less insulin resistance, more beta cell mass deficit and less possibility to be influenced by the surgical changes in the gastrointestinal tract. That is reason why the first results on bariatric surgery for treating diabetes published by the first author of this review were in this group of patients. It was no reason to believe that the effect on DM resolution of surgical gastrointestinal changes in patients BMI < 35 could differ from those in patients BMI > 30. The difference between both are some kilograms but both are obese (morbid or simple obesity) and part of the type 2 diabetes is due to the insulin resistance linked to the lack of capacity of adipose tissue to store more fat and the consequent high amount of circulating fatty acids. Even in diabetic patients with BMI < 30 the fat distribution (more visceral than subcutaneous as it seen at surgery) can condition the progression of insulin resistance to develop type 2 diabetes and could explain the parallel postoperative evolution of DM in morbid obese (BMI > 35), simple obese (BMI 30-34) and non obese (BMI < 30) diabetic patients after bariatric surgery with the intention of solving their diabetes melitus. As well as that the results are in all cases more related to years of evolution of DM, non insulin treatment, years of insulin treatment and preoperative Peptide C levels, than to preoperative BMI.

The same results were also reported by all the few clinical experimental studies included DM patients below BMI 30 existing in the literature.

Initially, only the concepts of intestinal modifications of the RYGB were used as well as performing a Duodenojejunal Bypass (DBJ), preserving the stomach and the pyloric mechanism without adding an element of restriction. As described by De Meester, the Duodenal Switch was used for the first time for the treatment of recurrent gastroesophageal reflux disease, and despite good metabolic outcomes without significant weight loss, the emergence of problems in gastric emptying probably due to the increase of GLP-1 and the need to restrict intake to contribute to the improvement of diabetes, lead to incorporate a Vertical Gastrectomy as in the Classic Duodenal Switch.

"Navarrete et al decided to call it Short Duodenal Switch (SDS) showing good results in 11 patients operated by laparoscopy with a Vertical Gastrectomy with a 60 Fr boogie, a biliopancreatic limb of 50 cm and an alimentary limb of 100 cm, with remission in 60% of patients and control in the rest of operated subjects, which is a little lower than the Classic Duodenal Switch and the Gastric Bypass. This difference could be due to the maintenance of part of the gastric antrum in the sleeve gastrectomy in comparison with the complete bypass of it obtained with the gastric bypass procedures. Garcia Caballero et al. using BAGUA with a gastric pouch bigger than in obese and excluding only 100 cm jejunum distal to Treitz ligation in 13 patients mean preoperative BMI 27, reported 77% DM2 remission (77% insulinindependent patients, 3 of them with Peptide C zero) with mean postoperative HbA1c 6.6% and mean SFG 100 mg/dl. And Kim et al. in Korea reported in 2011 a prospective serie (mean preoperative BMI 27,2) with 70% DM2 remission and mean HbA1c 6.7% using MGB with a gastric pouch of 150-180 ml.

These results are also comparable with De Paula findings despite the patients baseline condition were not so severe: younger (mean age 51 years and 63 in Garcia caballero serie), 44% using insulin vs 77% and shorter DM evolution (more than eleven years vs 16 years in Garcia caballero serie) could have 95% well controlled without medication and HbA1c < 7% and 65% remission after two years of follow-up. The patients reach a postoperative BMI near 21 as Garcia-
caballero serie with BAGUA and had quite similar metabolic results 65% vs 77% DM remission. 40

So we have different gastrointestinal procedures to treat DM patients BMI < 30: BGYR,21 BAGUA,42 MGB,46 DJB without Gastrectomy,47 BDJ with SG or SDS,52 ideal interposition JJ or DI type54,55 and BPD56 and we do not fully know all the mechanisms involved in the control of carbohydrates metabolism after these surgical procedures? However, the results of the published series including low BMI DM patients54,56 have been very consistent in terms of their effectiveness and low morbidity, with rates of improvement, control and remission totally superior to those obtained by conventional medical therapy.57,60

Different surgical gastrointestinal changes and their influence in the possible mechanisms for controlling carbohydrates metabolism

Among other aspects, the dietary restriction, imposed by most of these bariatric surgical procedures, is one of those mechanisms since it is well known that the mere decrease of caloric intake improves diabetes.26,63 But biliopancreatic diversion procedures as gastric bypass, exclude the duodenum and jejunum from the alimentary circuit, but not restrictive techniques, can abolish type 2 diabetes within days of surgery, even before any significant weight loss has occurred. This means that calorie restriction alone cannot entirely account for this effect.

The complex hormonal changes that occur when altering the small intestine anatomy are undoubtedly one of the most studied findings of these and other surgeries.47,55 A gastric bypass, a biliopancreatic derivation or a duodenal-jejunal bypass, and before the patients lose weight significantly, there is an increase in the values of certain incretins (mainly GLP-1 and PYY), which translates into a better glucose homeostasis.57-61 These results were reproduced more accurately in the experimental studies of Rubino1,59 (theory of the upper intestine) and De Paul1,62 (theory of the lower intestine).

It is important to highlight that the changes of intestinal anatomy to bypass the upper part of the gastrointestinal tract seems to improve 2 or 3 times the mass and function of the pancreatic beta cell.61,64

These effects suggest that the intestine is itself involved in the immediate regulation of carbohydrate homeostasis throughout an increase in insulin sensitivity, disappearance of hypertriglyceridemia and decrease in levels of circulating fatty acids, disappearance of the mechanisms of lipotoxicity in the liver and skeletal muscle, changes in the activity of digestive vagal afferents and changes in intestinal flora, all of them mechanisms that need to be studied in greater detail.61

Procedures that involve the resection of the gastric fundus like the vertical gastrectomy, cause a significant decrease in the levels of ghrelin, creating better conditions for the control of glycemia, as has been reported in experimental studies by Li et al.85 and by Peterli et al.54 in diabetic obese patients. Recently Chronaiou et al have observed that adding a fundectomy to the BGYR produce a high elevation of the GLP1 and PYY hormone effect to the decrease of ghrelin, achieving a persistence of this phenomenon is attributable to the decline of this hormone.87

The group of Mithieux (see also his chapter in this issue) recently published a study in experimental models, which suggest the existence of a sensitive hepato-portal pathway which might explain part of the beneficial effects on the control of glycemia after these procedures.88,89

So it exits a physiological basis, although nascent, that begins to unveil the physiology of metabolic surgery, specifically that related to the treatment of type 2 diabetes.

Final remarks

The results of the series published in patients with a BMI < 30 allows us to affirm that gastrointestinal surgical procedures are effective also in this group of patients, and that while these are short-term studies of 1 and 2 years of follow-up, the outcome is comparable to that observed in patients with severe obesity, so it is reasonable that long-term behavior will be also similar.

Although recurrence of diabetes has been reported after 3 years in some patients who had experienced remission after a gastric bypass90,91 the possibility of delaying the occurrence of serious diabetic complications by 5 or 10 years represents a breakthrough for patients and society.

A special mention and consideration in our Western countries should be done about non-obese patients with type 2 diabetes like Scopinaro85 and other authors90,92,93 very well pointed out. Apparently, the metabolic response in these subjects is different since the improvement in glycemic control is not as good as in obese subjects BMI > 30, so this is not the only element to be considered.1 Other factors like anti-GAD antibodies, C-peptide,1,47,51 time of progression of the disease,12,94 age1,27 and some others already outlined in the introduction of this issue as minimum necessary information from the patients, should be taken into consideration as well as probably many other factors unknown to us in the light of current knowledge.

From all existing bariatric procedures, the laparoscopic gastric bypass and the gastric band are the most proven. The first being the most effective but with higher morbidity. Major complications are rare and mortality is rather exceptional, so it can be considered a safe surgery in these regards.14,16

Also, patients do not lose excessive weight so nutritional complications are not relevant.

The performance of the Duodeno-Jejunal Bypass should be considered in the management of patients
with a BMI < 30 because of its excellent results, especially since the volume of restriction of the vertical gastroplasty is greater in selected patients, always aware that it is a more complex surgery and a more expensive one with longer hospital stay and greater morbidity. A tailored BAGUA could be also a good alternative in the management of this patients with lower risk and costs and even superior results.

It is important to note that weight loss achieved by RYGB with a gastric pouch of 50 ml in patients with a BMI30-34 compared with the duodenojejunal bypass SG 160 ml associated with the equal length of limbs (biliopancreatic limb 50 ml and alimentary limb100 ml) in patients with BMI < 30, is statistically significant. Therefore it is recommendable to associate less restriction to lower BMI and again can also be considered the possibility of a BAGUA or a minigastric bypass. The ileal interposition although had good metabolic results, seems more complex to perform and more expensive.

Based on the analyzed results, gastrointestinal surgery for type 2 diabetic patients with a BMI 24-34 is an alternative that should be part of the therapeutic options, especially in patients that conventional medical treatment is unable to provide adequate control of the disease.

Not all meta-analysis studies are suitable, for which not all meta-analysis studies are suitable, for which conducting controlled studies with greater samples and long-term follow-up becomes essential, in order to establish whether the surgical option may be routinely recommended. And reaching a consensus among the different medical and surgical specialties in order to provide the best therapy against one of the most devastating diseases today.

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